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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,682	10/24/2001	Alan P. Wolffe	8325-0015.20	1541

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EXAMINER	
ZHOU, SHUBO	
ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
12/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/083,682	WOLFFE ET AL.	
	Examiner	Art Unit	
	SHUBO (Joe) ZHOU	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-71 and 125-128* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-71 and 125-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment/Status of the Claims

Applicant's amendment filed 8/13/09 is acknowledged and entered.

Claims 1-65 and 72-124 have previously been canceled, and claims 66-71 and 125-128 are presently pending and under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under

37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 66-71 and 125-128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clontech (Clontech Catalog, 1998-1999, pages 177-183, Clontech Laboratories, Inc., Palo Alto, California) in view of Grosveld et al. (US patent 5,635,355, Jun 3, 1997).

The rejection is reiterated from the previous Office action mailed 5/27/09.

In the previous Office action mailed 5/27/09, it is noted that all the above references had been provided to applicants during the prosecution of the application, and the rejections in the previous Office action mailed 3/31/05 had been affirmed by the Board of Patent Appeals and Interferences in a decision mailed 9/15/08.

In the previous Office action mailed 5/27/09, it is also noted that in the amendment filed 12/29/08 following the Board's decision, the claims were amended such that the claims are drawn to a library instead of a polynucleotide, and that each polynucleotide of the library comprising a vector and an insert, and each insert sequence consists essentially of accessible regions of cellular chromatin.

The claims, as currently written, are product-by-process claims.

The court in *In re Thorpe 777 F.2d 695, 698, 227 USPQ 964,966 (Fed. Cir. 1985)* holds:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The

> patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Clontech Catalog discloses multiple genomic libraries made from different organisms with cellular chromatin using different vector systems. See pages 177-183, especially the table on pages 182-183. These genomic libraries are made by a method involving digesting the whole genomes of the chromatin of different organisms with Sau3A I or Mbo I, which are four cutters and are known to digest the genomes with high frequency, and cloning the digested fragments in different vector systems. See page 177. It would be readily apparent to one of skill in the art that the libraries produced by such a method inherently comprise clones that have an insert that either consists of polynucleotide from regions of cellular chromatin that are accessible to reagents such as nuclease and restriction enzymes, as recited in claims 125-128, and that such libraries should comprise clones with an insert that comprises polynucleotides from the accessible region and the inaccessible region. The catalog discloses a plurality of libraries comprising polynucleotides from cellular chromatin of cells at a particular stage of the development, such as from mouse of ages of 9-11 weeks, and adult, and a plurality of libraries comprising polynucleotides from a particular tissue, such as mouse kidney and mouse liver. See the listing of genomic libraries on pages 182-183.The catalog also discloses a plurality of libraries comprising polynucleotides from healthy and diseased cells, such as normal muscle of Xenopus laevis and human Hela S3 cells (from ATCC#CCL2.2, see page 182), which are diseased (cancer) cells and infected with

viruses. See the previously provided page 1 of 3 of the printout of ATCC catalog from ATCC's website: http://www.atcc.org/SearchCatalogs/longview.cfm?atccsearch=yes.

Clontech Catalog does not disclose any library where each polynucleotide therein has an insert and each insert consists essentially of accessible regions of cellular chromatin. In other words, in the libraries of Clontech Catalog, there are inserts that do not consist essentially of accessible regions of cellular chromatin.

Grosveld et al. teach a method of preparing nucleic acids which comprise regulatory sequences from a cell (see column 21, claim 1, line 1, for example). The method involves treating isolated nuclei that comprise chromatin with DNaseI, where the enzyme reacts with accessible regions of cellular chromatin (see column 8, lines 17-21), fragmenting the chromatin with a restriction enzyme to generate DNA fragments (column 8, lines 23-25, and contacting DNA fragments of interests from precloned plasmids that contain DNase I hypersensitive sites with a population of vectors to permit ligation of the DNA fragments in order to use it for in vivo introduction. See column 8, lines 1-25, and column 15, lines 43-47. While Grosveld et al. do not clone the DNase I hypersensitive fragments identified in column 8, Grosveld et al. expressly suggest doing so because they expressly claim "a method of obtaining a DNA fragment comprising a dominant activator sequence, comprising providing a candidate DNA fragment comprising a Dnase I hypersensitive site from a genetic locus" …, and "ligating the fragment to an expressible gene to form a construct." Such DNase I hypersensitive fragments should encompass fragments from readily available clones or from the fragments identified in column 8. See claim 1.

One of ordinary skill in the art would have been motivated to modify the method of Clontech and motivated by Grosveld et al. to treat the chromatin with the method of Grosveld et al. and not only clone the DNase I hypersensitive fragment from a readily made clone containing such fragment if the clone is available, but also to clone the Dnase I hypersensitive fragments directly from the fragments identified in column 8 if there are no clones readily available comprising such fragments in order to obtain such fragments which contain regulatory sequences because Grosveld et al. claim and suggest obtaining such fragments. There would have been a reasonable expectation of success because such experimental methods of cloning and sequencing fragments of Dnase I digests would have been routine.

Applicant's arguments filed 8/13/09 have been fully considered but they are not persuasive. Applicant argues that neither of the reference teaches a library comprising essentially of inserts corresponding to accessible regions. This is not found persuasive. Although applicant provides arguments as to neither of the single references teaches the library, no argument is provided as to the examiner's position that Grosveld et al. suggest such cloning and such clones because, as set forth above, they expressly claim "a method of obtaining a DNA fragment comprising a dominant activator sequence, comprising providing a candidate DNA fragment comprising a DNase I hypersensitive site from a genetic locus" …, and "ligating the fragment to an expressible gene to form a construct" (see claim 1 therein), and such DNase I hypersensitive fragments should encompass essentially fragments from readily available clones or from the fragments identified in column 8 and such constructs, collectively, are a library, as would be readily apparent to one of ordinary skill in the art of molecular cloning.

Applicant then argues that Grosveld et al. fails to teach the recited method steps required to obtain these libraries as in claim 66. This is also unpersuasive because the method of claim 66 comprises contact the chromatin with a probe that cleaves accessible regions, then deproteinize the cleaved chromatin, and then digested with a nuclease to generate a collection of polyncucleotides. The method of Grosveld et al. in fact comprises these step as, admitted by applicant in the response on page 6, their method comprises treating nuclei, which comprises chromatin, with DNase I, which is a nuclease, but is also a probe based on the definition and examples of "probe" in the instant application (Instant claim 125 actually claims that the probe is a nuclease), then deproteinize the cleaved chromatin, and then digest them with Asp718 or BglII to generate a collection of polynucleotides, where the Asp718 or BglII is a restriction enzyme, which is also a nuclease (Again, the instant claim 126 claims that the nuclease is a restriction enzyme).

Claim Rejections - 35 USC § 112

The rejection of claims 125-128 under 35 U.S.C. 112 , second paragraph, set forth in the previous Office action is withdrawn in view of the amendment filed 8/13/09.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL.

Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136 (a). A shortened statutory period for response to this final action is set to expire

three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Shubo (Joe) Zhou/

SHUBO (JOE) ZHOU, PH.D.

PRIMARY EXAMINER